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PAGE 1 OF 7

FDA Panelists Suggest Some Changes To EPO Prescribing

By Aaron Lorenzo
Washington Editor

SILVER SPRING, Md. – Members of the FDA’s Oncologic Drug Advisory Committee on Thursday agreed to some degree with recent label changes to Amgen Inc.’s blockbuster EPO products, but also suggested a few further steps, proposing more studies and stricter guidelines on prescribing the red blood cell boosters.

Clearly, the latter recommendation stands to roil sales, as the FDA typically follows the advice of its panels, and a more conservative label could dampen further already slowing EPO use. Amgen’s stock (NASDAQ:AMGN) dropped 9.1 percent Thursday, or \$5.77, to \$57.33, not far off the two-year low the shares hit last month.

Richard Pazdur, the director of the FDA’s Office of Oncology Drug Products, declined to specify when
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Altus Starts Phase III Studies Of Pancreatic Enzyme Product

By Trista Morrison
Staff Writer

With the initiation of a pair of pivotal efficacy and safety trials for ALTU-135, Altus Pharmaceuticals Inc. is gearing up to enter the \$750 million worldwide pancreatic enzyme replacement market.

ALTU-135 still has a way to go before it enters the fray. Top-line data from its Phase III efficacy trial are expected in the second quarter of 2008, followed by data from its Phase III safety trial and a U.S. regulatory filing in the first half of 2009. But when ALTU-135’s time does come, the drug could capture up to 50 percent of the market, according to a report from analyst Joseph Schwartz at Leerink Swann and Co.

That’s because ALTU-135 would be the first microbially derived, recombinant option in a world of porcine-derived
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The Curious Case Of The Missing Stem Cell

New Lineage Tracing Method Finds No Pancreatic Stem Cell

By Anette Breindl
Science Editor

In many minds, regenerative medicine is synonymous with stem cells. And Type I diabetes, which is due to the lack of a single cell type – insulin-producing pancreatic beta cells – is a good candidate disease for the approach.

Recent findings suggested, though, that for replacing beta cells, the exact type of regenerative medicine may turn out to be different than expected.

In the May 2007 issue of *Developmental Cell*, scientists from the University of Pennsylvania School of Medicine report that in animal studies, they were unable to track down an adult stem cell that divides to produce insulin-producing pancreatic beta cells; instead, most, if not all, adult beta cells can continue to divide slowly.

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NEW CO NEWS

CalciMedica Gains Access To Programs In Calcium Channels

By Trista Morrison
Staff Writer

CalciMedica Inc. is carving out a niche in the autoimmune and inflammatory field by focusing on calcium release-activated calcium (CRAC) channels, which are critical to the release of interleukin-2, TNF-alpha and other cytokines involved in the immune response.

Back in 2005, scientists at TorreyPines Therapeutics Inc. pinpointed the *STIMI* gene as a key connection between the release of stored calcium and the activation of CRAC channels. Not long afterward, scientists at Harvard Medical School’s CBR Institute for Biomedical Research Inc. (CBRI) discovered a CRAC channel called

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*Financings Roundup***ProCertus Completes Series A Financing For Cancer Programs****By Jim Shrine
Staff Writer**

ProCertus BioPharm Inc. closed on its \$2.23 million Series A round of financing to fund development of products to protect cancer patients against the side effects of chemotherapy and radiotherapy.

ProCertus, of Madison, Wis., is developing ProDermaCel for chemotherapy- and radiotherapy-induced alopecia (hair loss), lead product DermX for radiotherapy-induced dermatitis (skin burn) and OralX for oral mucositis.

The company said it plans to begin Phase I/II trials this year to demonstrate proof of concept in humans.

The financing was led by Venture Investors LLC, which was joined by existing investors, including Novartis Venture Fund.

In other financing news:

- **StrataGent Life Sciences Inc.**, of San Jose, Calif., closed a \$6.65 million tranche of a planned \$16 million Series B financing round. The round was led by Essex Woodlands Health Ventures, and included Series A investor Quantum Technology Partners and Aphelion Capital. Remaining funds are tied to achievement of milestones. StrataGent is developing products based on its microjet technology, which is designed to deliver large and small molecules without a device penetrating into or through the skin.

- **Morria Biopharmaceuticals plc**, of London, raised £1.6 million (US\$3.8 million) through a private placement of 2 million shares at £0.80 per share. The round was led by its financial consultant, London-based Charles Street Securities Inc. Funds will be used in development of Morria's two leading drug candidates, MRX6, a topical formulation for treating contact dermatitis, and MRX4, an inhaled nasal spray for treating allergic rhinitis.

- **Progen Pharmaceuticals Ltd.**, of Brisbane, Australia, completed the sale of 6.9 million shares of common

stock at \$4.75 per share, raising gross proceeds of \$32.8 million (A\$39.7 million). Shares were sold from a shelf registration to institutional and other investors. Thomas Weisel Partners LLC was placement agent. The company previously said it intended to raise another \$28.2 million through a 1-for-9 rights issue. (See *BioWorld Today*, May 4, 2007.)

- **Sernova Corp.**, of Kelowna, British Columbia, raised \$2.4 million through the exercise of all outstanding warrants. Funds will be used to continue development of Sertolin, Sernova's cellular therapy for diabetes. About 4 million warrants were exercised at \$0.60 per share. Sernova also said it now has met all financing commitments for the Sertolin technology, giving it sole control of the product.

- **PolyMedix Inc.**, of Philadelphia, filed a registration statement relating to a proposed offering of up to \$35 million of common stock and warrants. Needham & Co. LLC is lead placement agent, with WBB Securities LLC co-agent. PolyMedix is developing synthetic small-molecule compounds that mimic the activity of large natural proteins, compounds referred to as biomimetics. Initial programs target infectious diseases and acute cardiovascular disorders.

- **EndoCeutics Inc.**, of Quebec, lowered the price range of its planned initial public offering to between \$7 and \$9 per share, down from an earlier plan of \$11 to \$13 each. The company still plans to sell 5.75 million common shares, which would raise \$46 if sold at the midpoint of the new price range. EndoCeutics registered earlier this year to raise up to \$75 million in an IPO. (See *BioWorld Today*, March 1, 2007.) ■

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EPO

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another label change could come for the products in question, known as erythropoiesis-stimulating agents (ESAs).

Committee members voted 15-2 that the products' continued marketing warrants some further label changes, and 17-0 that additional safety studies are needed. Among suggested boundaries, they voted 12-5 that labeling should restrict ESA use in certain cancers such as breast, non-small-cell lung and head and neck, given existing data. In addition, they voted 15-2 that labeling should set a hemoglobin level to begin ESA use in asymptomatic patients, and 16-1 for discontinuing ESA use after chemotherapy.

"There certainly are some more restrictions on the horizon," said Dhesh Govender, an analyst with Monness, Crespi, Hardt & Co. Inc. in New York. Expecting patients to end ESA treatment "much quicker," he boldly forecasted a sales erosion of up to 25 percent for Aranesp (darbepoetin alfa), which would amount to about \$1 billion. Govender, whose firm does not make a market in Amgen's stock, predicted the negative outcome earlier this week.

In addition to Aranesp, the products also include Epogen (epoetin alfa) and Johnson & Johnson's Procrit (epoetin alfa). Approved as supportive-care drugs to treat anemia in patients on chemotherapy and those with chronic kidney failure, a number of studies have since shed light on safety issues showing that higher-than-recommended doses can lead to multiple complications.

However, the committee members voted 11-6 against targeting a hemoglobin level lower than 12 g/dL, which seemingly contrasts with their other suggestions.

That left Chris Raymond, an analyst with Robert W. Baird & Co. in Chicago, feeling more sanguine about drastic sales slumps. As a result, he's modeling a \$100 million slippage in Aranesp sales this year compared to last year's \$4.1 billion in sales, and down \$300 million more next year, before beginning to climb again.

"I found it odd that the panel would completely brush by that upper-limit issue [beyond 12 g/dL], which is where all the controversy and safety issues exist," Raymond told *BioWorld Today*, though he later added that the committee consensus would "give the FDA a little more confidence if they really want to get very restrictive."

Still, he said the agency would presumably need more concrete data than are currently available to make sweeping changes.

Pazdur promised "internal discussions" to come at the FDA.

The central question before the committee related to whether problems associated with excessive ESA administrations signal the potential for worrisome outcomes when the products are dosed within the limits of their label. Both FDA staffers and Amgen officials presented a range of evi-

dence to back up their respective cases.

FDA medical officer Vinni Juneja outlined data from six studies that point to decreased survival, increased tumor promotion and higher numbers of thrombovascular events in patients with several types of cancers. In those trials, ESAs were administered to target hemoglobin levels that exceed 13 g/dL, a higher threshold than that recommended in the products' labels, or received by patients not getting chemotherapy.

"ESAs do not increase survival and may promote tumor growth," Juneja said, so in light of those risks, coupled with a better reputation for blood transfusions than when ESAs first received approval, he urged a "reconsideration" of their risk-to-benefit profile in cancer patients.

Juneja also warned against using meta-analyses to elucidate safety signals.

On the other hand, Amgen's executive vice president of research and development, Roger Perlmutter, noted that despite a longstanding acknowledgement of thrombovascular events due to ESAs, he said their benefits in this setting "are substantial and unambiguous."

In particular, he and other supporters noted the 50 percent reduction in blood transfusions in patients treated with ESAs, beneficial to their overall health outcomes and quality of life, as well as the nation's always-short blood supply. Further, Perlmutter said the erythropoietin receptor gene is not an oncogene and therefore not driving tumor growth. Other data point to a neutral survival effect for ESAs.

Urging panelists to review the totality of evidence from many more studies than the FDA cited, he stressed that ESAs have "no demonstrable effect" on overall survival or tumor progression when used in accordance with their label.

Additional committee ideas included corrective advertisements that amend prior promotions that suggest the products' beneficial impact on fatigue, an outcome that's not on their label, as well as placebo-controlled safety studies. A skeptical Govender told *BioWorld Today* that it would be "almost impossible" to prod Amgen into completing such testing, though Raymond noted inherent recruitment difficulties for those types of trials, given the longstanding use of ESAs.

His firm makes a market in Amgen's stock.

The products' recently revised labeling includes more conservative prescribing instructions to advise doctors to monitor hemoglobin and adjust doses to maintain the lowest level necessary to avoid blood transfusions. The change is underscored by a black box warning that ESAs increase the risk of death and cardiovascular problems when dosed to target hemoglobin levels above 12 g/dL.

Perlmutter said Amgen does not advocate exceeding such a threshold.

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Altus

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products. "If you look at the history in other markets, recombinant products almost always take the lion's share of the market over animal products," said Jonathan Lieber, vice president, CFO and treasurer at Altus.

ALTU-135, a blend of lipase, protease and amylase created with Altus' protein crystallization technology, could offer less variability than its porcine-derived competitors. Additionally, it is dosed in a single pill at every meal or snack while competitive products require four to five pills at a time.

The Phase III efficacy trial, in which the first patient has been treated, is a multicenter, randomized, double-blind, placebo-controlled study in about 150 cystic fibrosis patients with pancreatic insufficiency. Patients will receive one capsule of ALTU-135 at each meal. The primary endpoint is the treatment of fat malabsorption as measured by coefficient of fat absorption. Secondary endpoints include the treatment of protein and carbohydrate malabsorption as well as a decrease in the weight and frequency of patient stools.

The Phase III safety trial, which Lieber said will begin enrolling this quarter, is a year-long, open-label study in 240 patients, many of whom will roll over from the efficacy trial. The safety of ALTU-135 will be evaluated based on adverse events, physical examinations, vital signs and standard clinical laboratory testing.

The pivotal trials are expected to enroll within nine months at 50 trial sites. The trials follow a Phase II study in 129 patients in which ALTU-135 was well tolerated and improved fat ($p < 0.001$) and protein ($p < 0.001$) absorption as well as carbohydrate absorption.

Altus originally had hoped to start its ALTU-135 pivotal program in the second half of last year, but a manufacturing complication in July caused the company to delay the trials and knocked a quarter of the value off the shares. On Thursday, the Cambridge, Mass.-based company's stock (NASDAQ:ALTU) dipped 22 cents to close at \$13.66. (See *BioWorld Today*, July 26, 2006.)

As of March 31, Altus reported \$101 million in cash, cash equivalents and marketable securities. That figure does not include a public offering completed in April that netted the company \$90 million. Lieber said Altus will use between \$55 million and \$65 million to fund operating activities in 2007, including the Phase III trials. (See *BioWorld Today*, April 20, 2007.)

If ALTU-135 proves successful, Altus plans to commercialize the drug in North America through an internal sales force of 70 to 80 representatives and managers. Most patients with pancreatic insufficiency also have cystic fibrosis, and Lieber estimated the company could cover the 115 cystic fibrosis treatment centers in the U.S. with about 35 reps. The remaining reps could be used to target chronic pancreatitis, an area in which Lieber said he sees "signifi-

cant expansion potential."

In Europe, the countries of the former Soviet Union, Israel and Egypt, rights to ALTU-135 are held by Dr. Falk Pharma GmbH, of Freiburg, Germany. Lieber said the companies are "in discussions as far as a development plan for how to best move the product forward in Europe."

The market currently is dominated by Creon (Solvay Pharmaceuticals Inc.), Ultrase (Axcan Pharma Inc.) and Pancrease MT (McNeil Consumer & Specialty Pharmaceuticals), but changes are afoot. In 2008, IPO hopeful Eurand International SpA expects to launch a competitive product.

ALTU-135 may not be the only commercialization opportunity for Altus. Late last year, the company opted for a co-promotion clause when it licensed North American rights to its crystallized human growth hormone drug ALTU-238 to Genentech Inc., of South San Francisco, in exchange for \$30 million up front (half cash, half equity) and up to \$140 million in milestones. The joint development committee has not yet released a timeline for Phase III trials. (See *BioWorld Today*, Dec. 21, 2006.)

In preclinical development, Altus' most advanced candidate is ALTU-237, a crystalline formulation of an oxalate-degrading enzyme to address a disease in which patients have too much oxalate.

Altus plans to file an investigational new drug application this quarter, begin a Phase I trial in the third quarter and complete the trial by the end of the year.

If the ALTU-237 trial goes well, Lieber said it should create a "good comfort level" regarding ALTU-236 for phenylketonuria and ALTU-242 for gout, two preclinical drugs that use a similar approach to ALTU-237. Altus expects preclinical proof-of-concept data with both of those drugs this year and will move one into the clinic in 2008. ■

EPO

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Aranesp, Epogen and Procrit are manufactured by the Thousand Oaks, Calif.-based company, though Procrit is sold by Johnson & Johnson, of New Brunswick, N.J. The products' first-quarter sales dipped in light of the surge in safety concerns of late, with lower reimbursement limits reflecting the recent label changes but also leading to patient access problems.

In that background, many members of Congress are exploring whether to decrease Medicare reimbursement as well.

Additional pressure on the products could come from a potential competitor, CERA (continuous erythropoietin receptor activator), which Basel, Switzerland-based F. Hoffmann-La Roche Ltd. is positioning to enter the market.

An FDA advisory committee will meet this fall to discuss the safety of ESA dosing in anemic renal failure patients, Pazdur said. ■

Stem Cell

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Senior author Jake Kushner, a pediatric endocrinologist at The Children's Hospital of Philadelphia, described the implications of the study: "This research tells us that we need to better understand what regulates the growth of beta cells, rather than searching for adult stem cells that give rise to beta cells," he said. (A recent study that used stem cell transplantation for the treatment of Type I diabetes used hematopoietic, or blood-forming, stem cells, which replace the immune system rather than beta cells.)

The authors investigated cell fates by extending a labeling technique known as thymidine analogue labeling. Thymidine is one of the four bases that make up DNA. By sequentially using two different thymidine analogues, the authors could distinguish between cells that had undergone several recent divisions – which would be indicative of a stem cell – and more slowly dividing cells.

Using their lineage tracing method, the authors were able to see adult progenitor cells in the intestines and skin, confirming that the method was able to identify stem cells.

But in the pancreas, such putative stem cells were nowhere to be seen. "Remarkably, we observe no contribution to adult beta cell mass by specialized progenitors or stem cells," the authors wrote in their paper. Instead, "we show that adult beta cells exhibit equal proliferation potential and expand from within a vast and seemingly uniform pool of mature beta cells."

The authors also found that even though most, if not all, adult beta cells appear to be able to divide, they apparently have natural brakes on how rapidly they are able to do so. In what the researchers termed a "replication refractory period," beta cells appeared unable to divide more than once every few months under normal circumstances.

Kushner told *BioWorld Today* that so far, the duration of the refractory period is unclear, but it appears to be between three and eight months. Studies to pin the timing down more exactly are ongoing, as are investigations into whether other slowly dividing adult tissues use a similar mechanism. The refractory period was shortened, but not abolished, under special circumstances – both in pregnancy and if part of the pancreas was removed surgically.

Since not all beta cells are destroyed in patients with Type I diabetes, the findings suggested that stimulating those residual beta cells to divide and conquer diabetes might be a viable therapeutic approach, though the refractory period they describe makes clear that the approach will have its own challenges – or as the authors put it, "efforts to determine the molecular regulation of adult beta cell proliferation are particularly strategic."

In the meantime, the method itself also opens new possibilities for lineage tracing. Current lineage tracing over several cell divisions requires the use of cell-surface markers, which limits the cell types that can be studied. Double labeling obviates the need for such markers, making it pos-

sible to study the lineage of a much wider group of cells, and search for dividing cells in an "unbiased" manner, the authors wrote. They foresee application in lineage tracing, but also in the study of stem cell divisions. The growth of cancer cells and the response to chemotherapy could be studied using the technique as well. ■

OTHER NEWS TO NOTE

• **Angiotech Pharmaceuticals Inc.**, of Vancouver, British Columbia, amended its agreement with **Edwards Lifesciences Corp.**, of Irvine, Calif., regarding the distribution of Angiotech's Vascular Wrap paclitaxel-eluting mesh/ePTFE graft combination product. Angiotech now has the exclusive rights to distribute the product through its own sales force and distribution network in Europe. Edwards still retains the same marketing and distribution rights with respect to the stand-alone Lifespan vascular graft product line as outlined in the original agreement.

• **Atrium Biotechnologies Inc.**, of Quebec, changed its name to Atrium Innovations Inc. The company said the name change reflects its evolution from being the subsidiary of a biotechnology company to a multiproduct manufacturer and marketer.

• **Biocrates Life Sciences GmbH**, of Innsbruck, Austria, said it is among the participants in a Framework Six European Union project named COBRED, a program to use innovative technology platforms to find diagnostic biomarkers for colon and breast cancers. Biocrates will bring its targeted metabolomics services platform, TargetIDQ, to the effort, which includes eight partners from France, Hungary, Estonia and Austria.

• **Biosite Inc.**, of San Diego, received a letter from **Inverness Medical Innovations Inc.**, of Waltham, Mass., contemplating an offer by Inverness to purchase, by way of a cash tender offer, all of the outstanding shares of common stock of Biosite not already owned by Inverness for \$92.50 per share. The letter was accompanied by a merger agreement signed by Inverness and copies of signed commitment letters from Inverness' proposed financing sources. The amount beats by \$2.50 per share an offer made by **Beckman Coulter Inc.**, of Fullerton, Calif. (See *BioWorld Today*, April 11, 2007.)

• **Cortex Pharmaceuticals Inc.**, of Irvine, Calif., and TEC Edmonton, on behalf of the University of Alberta, entered an exclusive patent license agreement that could broaden the use of Cortex's Ampakine technology to prevent and treat opiate- and barbiturate-induced respiratory depression. University of Alberta work has shown through in vitro and in vivo animal models that selected Ampakine compounds can enhance respiratory drive and breathing rhythm at the level of the brainstem. While few adverse drug events caused by prescription medications are respiratory in nature, they account for 25 percent to 30 percent of drug-induced deaths, it said.

CalciMedica

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Orail, which is believed to work with STIMI as a gatekeeper of the Icrac pathway and be a valid drug target for immunosuppression.

But the inflammatory disease implications of STIMI and CRAC channels fell outside of TorreyPines' focus on the central nervous system. "We just weren't using the IP," said Neil Kurtz, president and CEO of TorreyPines.

TorreyPines' vice president of research and drug discovery, Gonul Velicelebi, approached Kurtz about founding a company around the STIMI program. Kurtz liked the idea of "creating value for investors" by selling off noncore assets.

In late 2006, Velicelebi obtained seed funding from SR One, and CalciMedica was born. On Monday, the La Jolla, Calif.-based start-up announced it licensed both the STIMI program from TorreyPines and the Orail program from CBRI.

From TorreyPines, CalciMedica gets several preclinical small-molecule CRAC channel inhibitors, intellectual property and specialized equipment in exchange for equity and potential future fees, milestone payments and royalties. From CBRI, CalciMedica acquired exclusive rights to Orail. Specific financial terms were not disclosed for either deal.

Over the next 12 months, Velicelebi – now president and CEO of CalciMedica – said her team will focus on advancing the licensed preclinical compounds toward the clinic and conducting additional discovery work to identify

novel scaffolds. While work in the area previously was complicated by the fact that CRAC channels have very small signals, CalciMedica will use its intellectual property and expertise to engineer cells that express STIMI and Orail at higher levels.

The exact timeline of moving into the clinic will "depend on financings," Velicelebi said, adding that the company is "working on a Series A now."

Velicelebi also may expand her three-person team, which currently consists of two other ex-TorreyPines scientists. She described CalciMedica's business model as a "hybrid" in which core calcium channel biology and chemistry work will be done in house while "commodity services" may be contracted out.

In addition to integrating its newly acquired assets, CalciMedica is keeping busy talking to autoimmune and inflammation experts to prioritize the applications of its technology.

The company is looking both at "big ones like rheumatoid arthritis and inflammatory bowel disease" and at the indications with a smaller patient population but a significant unmet need, Velicelebi said.

CalciMedica is one of the only companies exploring CRAC channel inhibitors against autoimmune and inflammatory diseases.

Synta Pharmaceuticals Corp., which priced a \$50 million initial public offering earlier this year, has a preclinical CRAC-inhibitor program, but Velicelebi said she is not aware of any other companies working in the space. (See *BioWorld Today*, Feb. 7, 2007.) ■

OTHER NEWS TO NOTE

• **CytoGenix Inc.**, of Houston, and **Eurogentec SA**, of Liege, Belgium, executed a letter of intent regarding synDNA development. They plan to collaborate to optimize manufacturing and to implement purification and quality-control parameters. A successful collaboration would facilitate submission of European Union regulatory filings with products containing synDNA. CytoGenix said it has developed a synthetic process for large-scale production of high-purity DNA.

• **Evotec AG**, of Hamburg, Germany, said **Panacos Pharmaceuticals Inc.**, of Watertown, Mass., extended its ongoing discovery collaboration with Evotec into its fourth year. Applying its expertise in medicinal chemistry, Evotec has supported Panacos since 2004 in identifying novel compounds for treating viral infection. Now, the program has been extended and expanded to include Evotec's development chemistry services. The development support includes the scale-up of selected compounds for development studies and the optimization of compounds before their selection for studies through

experiments such as salt screens.

• **Gene Logic Inc.**, of Gaithersburg, Md., entered an agreement with **Abbott Laboratories**, of Abbott Park, Ill., to use its repositioning technology to seek additional development paths for multiple Abbott drug candidates, all of which have successfully passed Phase I human trials. Gene Logic is entitled to milestone payments for each drug candidate Abbott returns to clinical development. In addition, it would receive royalties on any resulting drug sales. Gene Logic also has the option to exclusively license any drug candidate Abbott chooses not to pursue, in which case Abbott would be entitled to milestone and royalty payments. Specific financial terms of the deal were not disclosed.

• **GenVec Inc.**, of Gaithersburg, Md., presented preclinical research demonstrating the ability of its new adenovector, Ad35, to induce and sustain protein production in the eye. GenVec researchers compared the duration of expression in the eye of two different adenovectors, Ad5 and Ad35. The results showed sustained protein expression beyond four months in eyes treated with the Ad35 vector. Results were presented at the Association for Research in Vision and Ophthalmology meeting in Fort Lauderdale, Fla.

CLINIC ROUNDUP

- **Manhattan Pharmaceuticals Inc.**, of New York, finished patient dosing in two separate, ongoing Phase IIa trials of oral oleoyl-estrone. The first trial is evaluating OE for common obesity, and the second targets morbid obesity. Both trials include a post-dosing follow-up period. Study completion and data analysis will begin after the final follow-up visit, and the analysis is scheduled to be completed in July.

- **Molecular Insight Pharmaceuticals Inc.**, of Cambridge, Mass., started a two-stage, Phase I/II trial with Azedra, also known as Ultratrace iobenguane I131 or Ultratrace MIBG, for malignant pheochromocytoma, a type of neuroendocrine cancer. The trial is designed to determine therapeutic dosing and evaluate the safety and efficacy of Azedra, a targeted radiotherapeutic that consists of the known I-131-MIBG molecule radiolabeled using the company's Ultratrace technology. The Phase I segment of the trial, which is expected to involve 12 to 18 patients, is a dose-ranging study designed to determine the maximum tolerated dose. The company expects that the dose-ranging portion will be completed in the second half of this year. In

the Phase II part, safety and efficacy of Azedra as a monotherapy will be tested, and up to 37 patients are expected to enroll in the U.S., Canada and Europe.

- **Repligen Corp.**, of Waltham, Mass., disclosed positive results from a Phase II trial with RG1068, synthetic human secretin, an agent to improve the assessment of pancreatic duct structures by magnetic resonance imaging. The study showed an improvement in sensitivity of detection of structural abnormalities of the pancreatic duct of about 20 percent, with no loss in specificity, consistent with prior data and expectations. Also, RG1068 yielded highly significant increases in three assessments: physician confidence in the ability to identify structural abnormalities, the number of pancreatic duct segments visualized and improvement in the overall quality of the MRI images.

- **Ziopharm Oncology Inc.**, of New York, dosed the first patient in a Phase II trial with ZIO-101 (organic arsenical) for the treatment of patients with primary liver cancer. The study will take place at five U.S. liver cancer treatment centers, including sites in New York, Boston, Miami, Seattle and Atlanta. Exposure to ZIO-101 has a direct as well as indirect effect on mitochondrial functions, resulting in depletion of energy supply to the cell and induction of apoptosis, the company said.

OTHER NEWS TO NOTE

- **Inno Biologics Sdn. Bhd.**, of Negeri Sembilan, Malaysia, entered a 10-year cooperation agreement with **Boehringer Ingelheim GmbH**, of Ingelheim, Germany, whereby Inno clients will have access to BI's manufacturing technology platform for Phase I and Phase II biopharmaceutical products produced by mammalian cell culture. Separately, Inno signed a five-year development and biomanufacturing contract with **Avesta Biotherapeutics & Research Pvt. Ltd.**, of Bangalore, India, under which Inno will provide pilot, clinical- or commercial-scale production for several of Avesta's pipeline molecules. In a third, separate deal, Inno entered a supply agreement with **Malaysian Bio-Diagnostics Research Sdn. Bhd.**, of Bangi, Malaysia, that involves supplies of antibodies from Inno to MBDR for use in diagnostic kits. Financial terms were not disclosed.

- **KineMed Inc.**, of Emeryville, Calif., received an option to exclusively license from the Massachusetts Institute of Technology intellectual property related to scavenger receptor-class B type I (SR-BI). Under the agreement,

KineMed has the option to exclusive rights to issued patents that cover SR-BI as a therapeutic target for the treatment of atherosclerotic heart disease. KineMed also got an option for nonexclusive rights to methods of screening for drugs that modulate SR-BI expression and activity, and genetic models of SR-BI modulation. Terms were not disclosed. Separately, KineMed offered animal-model data on a method for measuring the efflux of cholesterol from tissues through reverse cholesterol transport, the only known mechanism by which excess cholesterol can be removed from tissues. Data, presented at the Arteriosclerosis, Thrombosis and Vascular Biology Annual Meeting in Chicago, compared the effects of several therapeutic approaches on RCT in real time with live animals.

- **Viropro Inc.**, of Montreal, and **Intas Biopharmaceuticals Ltd.**, of Ahmedabad, India, signed a memorandum of understanding for the production of an undisclosed therapeutic protein. As a result of the commercial and research collaboration, Intas will invest equity in Viropro, and pay a licensing fee for the development and technology transfer of the manufacturing process. Viropro also gets royalties, and both firms will be able to out-license the process, sharing royalties from third-party manufacturers.

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